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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HAMA, JOANNE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/824,448	WEISS ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 14-39* is/are pending in the application.

4a) Of the above claim(s) *14-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Rejection of May 23, 2006 on August 28, 2006. Claim 39 is amended. Claim 13 is cancelled. Claims 14-38 are withdrawn.

Claims 1-12, 39 are under consideration.

Information Disclosure Statement

Applicant has indicated that the dos Santos et al. and Schaeffer et al. references have been submitted on August 25, 2004 and appear to be attached to the Scott et al. reference. The Examiner has acknowledges that the dos Santos et al. and Schaeffer et al. references were submitted August 25, 2004 and that Applicant has also provided additional copies of dos Santos et al. and Schaeffer et al. at the end of Applicant's response, filed August 28, 2006. The objection to the IDS has been withdrawn.

Withdrawn Rejections

35 U.S.C. § 112, 2nd parag.

Applicant's arguments, see page 17 of Applicant's response, filed August 28, 2006, with respect to the rejection of claim 39 have been fully considered and are persuasive. Applicant has amended the claim from "agent" to "test compound." The rejection of claim 39 has been withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-12, 39 remain rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility for reasons of record, May 23, 2006.

Applicant's arguments filed August 28, 2006 have been fully considered but they are not persuasive.

Applicant indicates that while the Examiner had indicated only three utilities of the claimed transgenic mice, that the assessment was incorrect. Applicant indicates that there are other uses of the claimed mice. On pages 69-73 of the specification, the AHSP knockout mice of the invention can be used in the production of AHSP antibodies (Applicant's response, page 12, 3rd parag.). In response, this is not persuasive because using the AHSP knockout mice to make antibody is not a specific and substantial use of the claimed invention as all knockout mice can be used to generate antibody against the protein encoded by the knocked out gene. With regard to Applicant indicating that the generated antibodies can be used to determine if an AHSP has been modified, such as by post-translational modification (Applicant's response, page 12, 3rd parag.), the argument, which pertains to use of an antibody, is not germane to the discussion, as the issue at hand is about a knockout mouse.

Applicant indicates that Example IV (pages 66-69 of the specification) teaches that loss of AHSP worsens beta-thalassemia and alpha-thalassemia, at least in mice (Applicant's response, page 13, 2nd parag.). In response, this is not persuasive because the issue at hand is whether the claimed mouse is a model for any human

disease. However, nothing in the specification teaches that disruption or loss of AHSP is associated with any human condition and thus, loss of AHSP in a mouse model is not readily apparent. Applicant indicates that the instant specification teaches that AHSP is well conserved in different species and that the pathological features of beta-thalassemia closely mimic the characteristics seen with AHSP knockout mice (Applicant's response, page 15, 1st parag.). In response, the fact that AHSP is well conserved in various species of animals is not indicative that the function of a protein is conserved in any species of animal; further, the fact that the knockout AHSP mouse exhibits a phenotype is not indicative that humans will exhibit the same phenotype (for further discussion, see Office Action, May 23, 2006, pages 8-9, Enablement rejection). Applicant indicates that the decreased expression AHSP worsens beta-thalassemia in humans and provides Galanello et al. as support. In response, Applicant's response is directed to mice comprising a homozygous disruption in AHSP and further comprising alpha and beta globin deficiencies; however, the claims are drawn to mice solely comprising a homozygous disruption in AHSP. Nonetheless, the mice comprising a homozygous disruption in AHSP and alpha and beta globin deficiencies also have no utility. The teachings of Galanello et al. are not persuasive because while Galanello et al. teach that thalassemia intermedia patients exhibit a 9.0 fold lower average expression in AHSP, as compared to beta carriers and normal subjects, Galanello et al. do not teach whether the reduction in AHSP expression is correlated with or causes the severity in beta-thalassemia. Further, according to post-filing, art, Viprakaset et al., 2004, Blood, 103: 3296-3299, teach that no mutation or specific association between

haplotypes of AHSP and disease severity in Hb E-beta thalassemia patients and thus suggests that AHSP is not a disease modifier in Hb E-beta thalassemia (Viprakaset et al., abstract). As such, an artisan cannot readily predict that AHSP has any role in human disease and the use of the claimed mouse as a model of human disease is not readily apparent.

Applicant indicates on page 49 of the specification, that Miele et al. teach that AHSP is downregulated in spleen, bone marrow, and blood of animals with transmissible spongiform encephalopathies (TSE) (Applicant's response, page 13, 2nd parag.). The antibodies generated via immunization of the instantly claimed transgenic mice could be used to assay a sample from an animal to determine the level of AHSP and to determine whether alpha or beta thalassemia would be exacerbated in a test animal or to determine whether an animal has TSE. In response, Applicant's arguments are not germane; the issue at hand is not about AHSP antibodies, but about use of the claimed AHSP knockout mouse.

With regard to the Examiner finding that the methods of using the claimed mouse lack utility, Applicant rebuts the Examiner's findings. Applicant indicates that the loss of AHSP has been associated, for example, with TSE and with the worsening of beta thalassemia and alpha thalassemia. As such, it is clear that the screening for and identification of compounds which restore AHSP activity or serve as a substitute for AHSP activity possesses utility as they may be used to lessen the symptoms of these diseases (Applicant's response, page 14, 2nd parag.). In response, these are not found persuasive. With regard to Applicant indicating that loss of AHSP has been associated

with TSE, nothing in the specification or the art teach that AHSP is causative of the disease. The specification indicates that EDRF (another name for AHSP) can be used as a diagnostic marker in TSE (specification, page 3, 1st parag.), but does not teach that EDRF has a role in progression of TSE. Note that the Office Action of May 6, 2005, page 20, has also discussed this issue. Regarding whether the claimed mice have utility in a screen for compounds to lessen the symptoms of TSE, the specification does not teach that the claimed mice exhibit any TSE. Whether the claimed mice exhibit TSE and could be used as a model for TSE is an issue and will be discussed further in the Enablement rejection. Regarding the use of the claimed mice to screen for compounds that lessen the severity of symptoms of alpha or beta thalassemia, the claims are not drawn to mice that have thalassemia. Further, the specification does not provide guidance that the mice are models of human disease and thus, the use of the mice for screening for compounds that reduce the severity of symptoms of alpha or beta thalassemia is not a specific and substantial use of the claimed mice.

Applicant indicates that a skilled artisan would find the three utilities cited by the Examiner, namely the use of the transgenic mice to understand the role AHSP plays in disease process, the use of the transgenic mice to establish a non-human model for the disease involving the under-expression or non-expression of AHSP, and the use of the transgenic mice to identify therapeutically effective agents, to be specific, substantial, and well-established utilities (Applicant's response, page 14, 4th parag. to page 15). In response, as indicated in the Office Action of May 23, 2006, pages 6-7, using the claimed mice to determine the role of a gene is not a specific and substantial use of the

claimed mice because research that involves studying the properties of the claimed product itself does not constitute a substantial utility. Further, such an asserted utility is a general utility as all knockout mice can be used to study the effects of loss of function of a gene that is disrupted. With regard to using the claimed mice as a model of human disease, neither the specification nor the art provide guidance that AHSP has a role in any human disease; thus, the claimed mice is not a model of human disease nor can they be used in screens to identify therapeutically effective agents.

For these reasons, the claims remain rejected.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12, 39 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record, May 6, 2005 and May 23, 2006.

Applicant's arguments filed August 28, 2006 have been fully considered but they are not persuasive.

As a first matter, the utility rejection, above, indicated that the claimed mice exhibiting TSE is an issue of enablement. As discussed in the Office Action of May 23,

2006, pages 8-9, the art teaches that the phenotypes of knockout mice were unpredictable. Further, the art did not consider the correlation between any observed mouse phenotypes and human disease as predictable. The cited art included Doetschmann et al., Moens et al., Jacks, et al., Kuehn et al., and Jaenisch et al. As this issue applies to the Applicant indicating that the claimed mice could be used in screens for compounds that could lessen the severity of symptoms of TSE, an artisan, based on the teachings in the art, cannot reasonably predict that an AHSP knockout mouse would exhibit TSE. Because the specification does not provide guidance whether an AHSP knockout mouse exhibits any symptom of TSE, an artisan cannot predict whether the claimed mouse is a model of TSE. As such, an artisan is not enabled to use the claimed mouse as a model of TSE.

Regarding the issue that because neither the specification nor the art provide guidance that the claimed mouse is a model of human disease, the enablement rejection as it applies to the claimed mouse and its use are maintained.

With regard to the Examiner indicating that, "nothing in the specification or the art indicates how to screen for agents that affect AHSP activity when the mice do not express AHSP," Applicant indicates that the test compounds or agents are screened for their ability to substitute for AHSP and restore AHSP activity. In response, while Applicant indicates that this is what meant by the claims, the claims are not read as such. The claims are drawn to agents that "affect" AHSP activity. According to the Merriam-Webster Dictionary [online], 2006 [retrieved on 2006-11-07], retrieved from Internet:URL: http://www.m-w.com/cgi-bin/dictionary, pages 1-2, "affect" means: to

produce an effect upon: as **a** : to produce a material influence upon or alteration in <paralysis *affected* his limbs> **b** : to act upon (as a person or a person's mind or feelings) so as to effect a response : **INFLUENCE**. Based on the definition of "affect," as in **a**, the therapeutic agent would need a target, i.e., AHSP protein. However, the mice of claim 1 have no AHSP protein, and thus, an artisan is not enabled to practice the claimed method. Based on Applicant indicating that that the agents are to substitute for AHSP activity, perhaps instead of using "affect," Applicant intended to mean "effect." According to the Merriam-Webster Dictionary [online], 2006 [retrieved on 2006-11-07], retrieved from Internet:URL: http://www.m-w.com/cgi-bin/dictionary, pages 1-2, "effect" means **1** : to cause to come into being **2 a** : to bring about often by surmounting obstacles : **ACCOMPLISH** <*effect* a settlement of a dispute> **b** : to put into operation <the duty of the legislature to *effect* the will of the citizens> **synonym** see PERFORM. Based on these definitions of "effect," in particular, **2b**, and with respect to what Applicant intended in the method of claim 9, it appears that "effect" is what is intended when using the claimed mice to screen for therapeutic agents. Because the claims read that the therapeutic agent affects AHSP protein, which is not expressed in the mouse of claim 1, an artisan cannot practice the claimed method and the rejection, as it applies to this claim is maintained.

For these reasons, the claims remain rejected.

Conclusion

No claims allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JH

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PRIMARY EXAMINER